NEWER ASPECTS AND METHODS IN THE STUDY OF THE MECHANISM OF THE HEART-BEAT.

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The interest now very widespread, in the physiology of the heart-beat developed from certain observations which Carlo Matteucci made some seventy-two years ago, and which he communicated in 1842 to the Academy at Paris. He established the fact that the muscle of a nerve-muscle preparation contracted if its nerve were laid across a second muscle which had been made to contract. He believed that the stimulus which the nerve received, and which it conveyed to its attached muscle was electrical in nature. Thirteen years later, in 1855, Kölliker and H. Müller widened the scope of Matteucci's observations by demonstrating in the same way that, if the nerve of a similar nerve-muscle preparation were laid across a heart, the muscle of the preparation likewise contracted, because, as in Matteucci's experiment, a current, called a current of action, was discharged from the contracting heart and was conveyed to the muscle.

These discoveries continue to be the primary subjects of experiment in contemporary studies in the mechanism of the heart-beat. The first experiments dealing with action currents were made by Marchand, Engelmann, and by Burdon-Sanderson and Page, who used a Bernstein rheotome in their investigations, but later the use of the capillary electrometer of Lippmann was introduced, especially by Marey, Waller, by Bayliss and Starling, Gotch and others. Marey in 1876 was the first to obtain permanent records of the action currents of the heart by photographing the motions of the meniscus of the mercury column of the electrometer on a moving sensitive surface. This record was a continuous curve in which could be distinguished various waves, one of which has been identified as synchronous with the contraction of the auricles, the upper chambers

of the heart, and certain others with the contraction of the ventricles, the lower pair of heart chambers. At first all records were obtained by applying electrodes directly to the surface of the heart as it lay exposed in the opened chest, but in 1889 Waller showed that one could obtain records of these currents by applying suitably constructed electrodes to the surface of the body without opening or injuring it. This discovery opened the way for studying these currents in the human subject. Waller also showed which were favorable and which unfavorable locations for placing electrodes, by varying the situation at which they were applied. From a consideration of records ob-

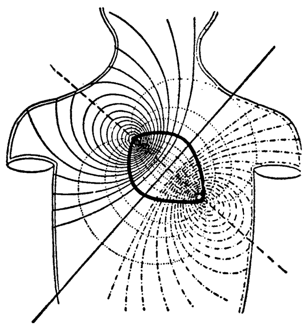

Fig. 1. After Waller. To indicate the spread of the cardiac action current through the human subject.

tained from a number of positions, now called leads or derivations, he determined the location of a plane, on the two sides of which the greatest differences in potential were developed (Fig. 1). Those locations were called favorable which yielded curves showing the largest waves, and the records were called electrocardiograms. The differences between electrocardiograms taken indirectly in this way and those taken directly from the surface of the heart are ones of contour and do not involve the important time relations of the various elements composing the curve.

With the knowledge that the heart discharged action currents, and a method for conducting these from the uninjured surface of the body to a registering instrument, the time was ripe for the construction of a galvanometer better fitted to the purposes of physiological and medical research. W. Einthoven of Leyden in 1902–6 described and built this instrument. Its completion at that time was

especially fortunate, for fresh discoveries in anatomy and physiology were almost simultaneously announced. In the interpretation of the significance of these, the galvanometric method of registration was especially valuable.

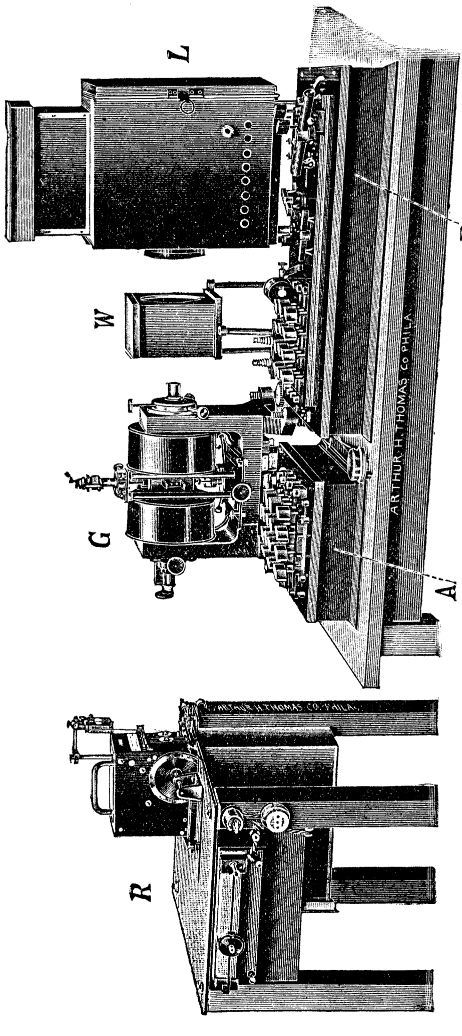

FIG. 2. String galvanometer, Edelmann's model. *R*, photographic recorder; *G*, galvanometer; *L*, arc light; *W*, water-bath; *A* and *B*, resistance and compensating boxes.

The principles Einthoven employed were in use in Deprez-D'Arsonval's instrument. From these he developed formulæ which formed the basis of the galvanometer he constructed. An instru-

ment built on similar lines for use as an ocean telegraph recorder had already been devised by Ader, but of this he was unaware at the time. It depends on the principle that a conductor suspended in a magnetic field is deflected at right angles to the lines of force when a current passes through it. The conductor chosen is usually a silvered quartz or platinum thread, 87 to 100 mm. long, 3 to 6 micra thick, having a resistance of 3,000 to 6,000 ohms It is suspended vertically between the poles of two powerful electro-magnets (Fig. 2). The thread is illuminated by the rays of an arc light which are focused on it by a system of lenses and a substage condensor. To accommodate this condensor the pole of one electro-magnet is bored. The motions of the string are magnified and projected on a recording photographic surface by a microscope held in a similar bore in the pole of the other electro-magnet. The degree of magnification may be varied according to the needs of the investigator, but, in order to maintain a degree of uniformity in the appearance and in the electrical value of curves obtained in different laboratories, certain arrangements have become conventional. These include the strength of the magnetic field, the tension of the string and its deflection time. The strength of the field depends, of course, on its construction. The tension of the string is adjusted in an appropriate manner so that a current having the value of one millivolt, when allowed to pass through it, causes a deflection of 1 cm. It has been found desirable to obtain a deflection of this extent within a definite length of time, usually 0.02 seconds or less. When the deflection time is longer, certain waves in the electrocardiogram tend to disappear.

But in order to obtain an electrocardiogram, more is necessary than to include an individual in the string circuit. For although the usual cardiac action current does not deflect the string, when it is at the prescribed tension, beyond the optical field, the skin or constant current, which is also continuously discharged from the body, and which is composed of the summed discharges from the other electrically active tissues of the organism, may do so, and it is usually sufficiently great to deflect the string far beyond the field of the microscope. This current does not show the rapid changes of potential difference that the action current from the heart does. On the

whole, its strength is uniform and changes so little within small limits of time as to render the change negligible. There is consequently no danger of confusing it with the rapid changes in electrical potential which compose the electrocardiogram. In order to keep the string in the optical field, from which the constant or skin current tends to deflect it, a system of compensation has been found necessary. This system comprises another source of current, a commutator and a series of resistances which are introduced into the string-heart circuit. The action current to be recorded, and with it the constant current, are permitted by a shunt to pass through the string in increasing amounts, so enabling one to allow a sufficient electromotive force of opposite polarity to the skin current to enter the circuit. Compensation in routine examinations becomes a simple procedure. To complete the records, a time curve and a millimeter scale are photographed on the record.

The most fruitful method of investigating the identity of the parts of the electrocardiogram has probably been that of recording synchronously on the same curve the electrocardiogram and mechanical curves representing the motions of the heart. As the result of these studies, it has been concluded that the contraction of the auricles is represented electrically by the *P* wave, the first wave in the cardiac cycle (Fig. 4), while the Waves *Q, R, S, T,* which follow it form a group in the electrocardiogram which are associated with ventricular activity. The term ventricular activity is purposely chosen, for there is as yet no uniformity of opinion in respect to designating which ventricular function it is which this complex of waves represents. Opinion is divided as to whether the complex represents the act of conduction, the state of muscular irritability, or actual contraction. It is doubtless unprofitable to analyze this discussion, and probably quite impossible to decide between these interpretations now. Of this much one can be certain, that the *QRST* complex does not occur unless the ventricles have been seen or known to contract. The significance of the individual waves of this group is also still a matter wrapped in doubt. Most writers favor the view that the wave *Q*, when present, signifies that the earliest ventricular activity has taken place near the apex of the heart, that the *R* wave represents the assumption of predominance

by the ventricular base, while *S* indicates a return of activity to the apex. The significance of the *T* wave is a hotly disputed point. Some hold it to represent the return of activity to the base of the ventricles in the later part of systole, because of an analogy which is drawn between the arterial base of the heart and the distal end of the primitive cardiac tube, which is, of course, the last segment to become affected by the wave of peristalsis which passes over it. The most important arguments against this interesting assumption have been supplied by Garten and his pupils, Clement and Erfmann. These investigators have all shown that the *T* wave occurs at the same instant of time at all points on the heart's surface, and refer its occurrence, as does also Einthoven, to a function inherent in muscular contraction. According to these authors, it represents the second wave in a current essentially diphasic. One need scarcely point out the fact that its presence simultaneously throughout the cardiac surface precludes the possibility of its occurring as the end phase of a peristaltic contraction.

Aside from the auricular representative and the group of waves representing ventricular activity, two other portions of an electrocardiographic curve must be described. The less debated of these is the portion following the *T* wave, the isoelectric period between the end of *T* and the beginning of *P*. It represents the diastole of the heart cycle,—from the end of the ventricular to the beginning of the next auricular contraction,—the rest period of the heart. The other portion is that lying between the wave *P* and the complex *QRST;* this portion also is usually isoelectric, but occasionally, as Einthoven has pointed out, its level departs from the base line. It is the period which represents the time occupied by the passage of impulses from the contracting auricles to the beginning of ventricular activity, and is called the conducting period.

We must now return to consider those other newer aspects of the study of the mechanism of the heart-beat to which I have referred in speaking of recent anatomical and physiological contributions. Before 1883 the theories held to explain coördination between the upper or auricular pair of the cardiac chambers and the lower ventricular pair consisted principally of an old notion of Haller's to the effect that the ventricles contracted in response to stimuli conveyed

to them by the act of filling, while others held and some do still that coördination between the two pairs rested on a carefully adjusted mechanism involving the passage of impulses over nervous channels. The need for theories of this sort lay in the fact that no muscular connection between the auricles and ventricles was known to exist. But in 1883, W. Gaskell convinced himself that the conduction of impulses in the heart must pass over muscular pathways, and Wooldridge and Tigerstedt contributed experiments which pointed to the

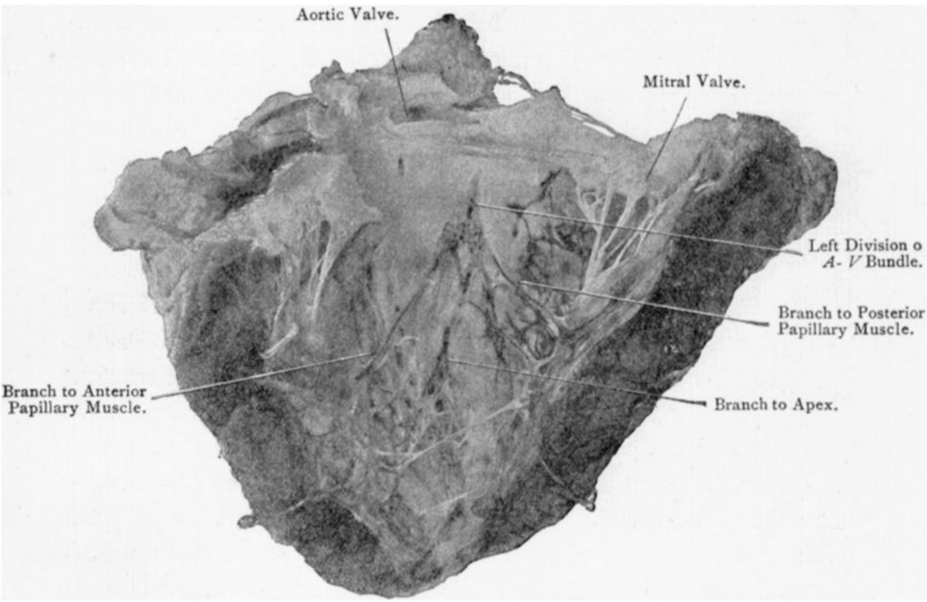

FIG. 3. Ox-heart. Injection with dilute India ink of the bursa-like spaces surrounding the left branch of the *A–V* bundle.

probability of Gaskell's contention. Ten years later (1893) Stanley Kent and His, Jr., actually saw and described a bundle of connecting muscular fibers. Since then (1893–1908) the existence of this structure, best called the auriculo-ventricular bundle, has been sufficiently confirmed. It passes from the lowest level of the auricles, divides into two and supplies a branch to each ventricle (Fig. 3). It has a peculiar muscular structure. In some species it contains large neural elements, but in man and the higher mammals only fine nerve fibrillæ

are found within it. With the establishment of the fact that the auriculo-ventricular bundle possessed this mixed structure, discussion as to whether conduction was nervous or muscular has gone out of fashion. Its essential function consists in conducting impulses and so coördinating the rhythms of the auricles and ventricles. To prove that it actually performs this function, its structure has been destroyed in experiments. In these the result anticipated was realized; auricles and ventricles continued to beat, each at a rate of its own and each in a rhythm without reference to the other. Two other facts are known about this bundle; first, that it can conduct impulses in a backward direction (from ventricles to auricles) as well as forwards; and second, that it conducts a little slower, especially at its upper terminal, than the rest of the heart muscle. We shall return to a consideration of this structure in relation to electrocardiography.

In 1906 another structure situated at the junction of the superior vena cava and the right auricular appendix was discovered by Keith and Flack. It is a small structure called the sino-auricular node. It has a sectional area of 0.3 by 0.1 cm., and attains a length of from 2.0 to 3.0 cm. Its existence has been abundantly verified. Like the conduction bundle, it also contains large and fine nerve elements. The comparative anatomy of both these structures has been traced by Ivy Mackenzie and by Külbs, while the embryology has been studied by Professor Mall. It is the discovery of these two structures, the sino-auricular node and the auriculo-ventricular system, which has added a second new and significant chapter to our store of information relating to the mechanism of the heart-beat.

The sino-auricular node has been recognized as the structure which usually initiates impulses for the contraction of the whole heart, and at the same time sets and maintains its rate. These properties have been attributed to it because excision or exclusion of the node from function reduces the rate of the heart-beat, and sometimes even stops it. Afterwards it begins gradually to contract again, but the original rate is not restored. It can usually be shown that another portion of the heart now sets the pace. Other methods have been employed to ascertain its functions; warmth applied to the site of the node accelerates the rate of the heart; cooling slows it. Attempts to alter the temperature elsewhere of the surface do not

have this effect. But more important information still is gained by means of the galvanometer. It has been demonstrated that each heart-beat begins at the node, because artificial contractions due to stimuli applied here yield curves of a shape identical with those resulting from spontaneous discharges; similar stimuli applied elsewhere fail of this identity. And finally, the law that the site at which contraction begins is primarily negative to other portions of the same strip of muscle is valid here. Lewis and Oppenheimer, Wybauw, Clement and Sulze have all been able to show that in contraction, the site of the node is primarily negative to all other portions of the auricular surface.

We have described the newly discovered structures in the mammalian heart. The function of the sinus node, in so far as it is now known, is to initiate impulses for the whole heart and to determine their rate; Lewis has aptly called it the pacemaker. The auriculo-ventricular bundle provides for coördination in the complicated mechanism of the heart. We must next show how, in the light of these structures, the electrocardiogram has been employed in elucidating the mechanism of the heart-beat. Althought the sinus node and the conduction bundle are very small indeed in comparison with the size of the whole heart, it is chiefly to these that the attention of investigators has been directed, while to the great mass of the organ which is charged with the real work of carrying on the circulation, very little research has been devoted. Our account of the electrophysiology of the heart must, therefore, be necessarily incomplete, and incomplete in just the direction in which one had hoped for light, —namely, in an attempt to employ electrical estimations as measures of the contractile force of the heart.

To be useful, the first demand of a method is that it give constant readings, and observation has shown that the electrocardiogram satisfies this demand, for its waves tend to remain unaltered in shape and size. When they alter, an ascertainable disturbance has in many cases been found as the cause. An electrocardiogram is, therefore, a reliable record. Its constancy is illustrated in records obtained from various classes of animals. They have certain characteristics in common, so that one can easily distinguish, for example, electrocardiograms of amphibia from those of the higher mammals. And

of the mammals, the species which have been studied, the horse, rabbit, cat, dog and man, each shows certain definite characters on the basis of which it can be recognized. Einthoven and Lewis and Gilder have studied human electrocardiograms and have defined within certain limits the usual form of curves taken from normal persons. But differentiation can go further, for the records of individuals have been found to differ widely from person to person in health, and more widely still in disease. Whatever form, either normal or abnormal, the curve assumes, this remains characteristic for the individual, for a certain length of time at all events, though the records be registered by different instruments and recorded by different investigators. An electrocardiogram may indeed attain a form so peculiarly personal that the suggestion has actually been made that it be employed to serve the purposes of identification in much the same way as the Bertillon system does. We may therefore regard the electrocardiogram as a valid and reliable record.

A number of the factors which can bring about variations from a normal curve are understood. Some of these may now be enumerated. The auricular wave, in the first place, is modified by the nature of the derivation or lead used; in this case the most favorable situations to employ are usually the two upper extremities, but under certain circumstances two points on the chest wall have been found preferable. A rare and not altogether satisfactorily established defect in the auricular mechanism is a lack of synchronicity between the contractions of the two auricles. This defect has occasionally been found to split the *P* wave. But the most significant alteration occurs when the *P* wave, instead of being directed upward, the direction which in the usual arrangement is associated with primary negativity at the site of the sinus node, is directed downward, an alteration which presumably shows that primary negativity has occurred at a lower level of the auricles. This change takes place when the sinus node is excluded from function, and when another part of the auricle sets the pace instead, but it also occurs spontaneously as the result of causes, the nature of which is not clear. It has been our good fortune to observe on a few occasions a gradual transition from *P* waves directed upward to *P* waves directed downward; if the apices of succeding *P* waves in such curves are joined, a curved line results.

This very curious phenomenon depends on an obscure mechanism, and unfortunately we have no satisfactory explanation for it. We know that where we have seen it best, it was associated with accidental intoxication by the drug digitalis. But we have seen indications of it in other connections which render its interpretation impossible with our present knowledge.

Some of the changes which are observed in the ventricular electrocardiogram are more easily explained. Considered as a whole, that is to say, in the light of the three usual leads of Einthoven (the first from the two arms, the second from the right arm and the left leg, and the third from the left arm and the left leg), one obtains a great many curves in which the waves in the first lead are inverted, and others in which inversion takes place in the third lead. Changes such as these result from a variety of causes. A heart which is not firmly anchored, but is easily shifted within the chest cavity by changes in the position of the body, may yield curves in which inverted waves appear. Comparable changes may result when the heart is pushed by air or fluid introduced in the chest, or when it is pulled to one or the other side by bands of adhesion stretched between the heart's surface and the chest wall. The explanation now offered for these phenomena by Einthoven and others is that the relation, determined by Waller, of the electrical axis of the organ to the body axis has become altered. Similar causes are probably at work in the electrical changes which are seen in increases in size of the heart, whether due to dilatation of its cavities, or to thickening of its walls; and the curves vary according to which side of the organ is involved. When the right side undergoes these changes, it is in the first lead that the ventricular waves become negative (Fig. 4); when it is the left side (Fig. 5), the negative waves appear in the third lead. Although alteration in the relation of the electrical axis and the body axis is the cause, that is to say, the mechanical, anatomical cause, commonly given for such deviations from the normal curve, it appears necessary to remember that in hypertrophy of the heart the balance of the sum of potential differences which produces the normal electrocardiogram must be disturbed, and that a rearrangement, that is to say, a functional rearrangement, of the parts of this sum must occur and might of course result in the changes we

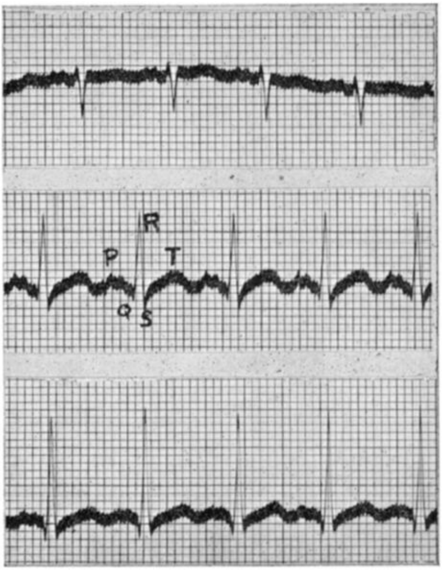

FIG. 4. Electrocardiogram showing the three usual leads of Einthoven. From a heart showing hypertrophy of its right ventricle.

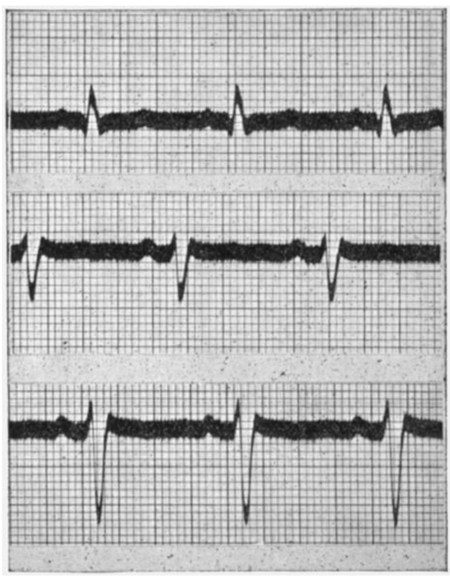

FIG. 5. Electrocardiogram showing the three usual leads of Einthoven. From a heart showing hypertrophy of its left vertricle.

are describing. More exaggerated changes still are observed when there is no alteration, either in the size or in the position of the heart; and these are due to the manner in which impulses are propagated to the ventricles from the contracting auricles. The pathway followed normally has already been described, but now the normal path cannot be taken, for it has been partly destroyed. It has been shown that when the conduction bundle to the right ventricle is

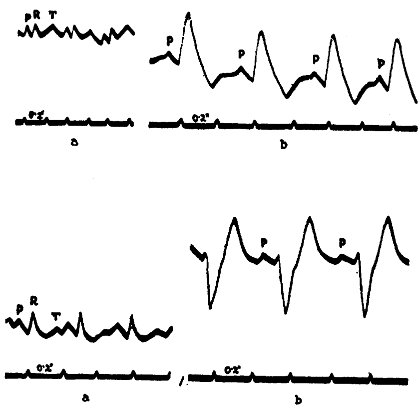

FIG. 6. Electrocardiogram from a dog. Leads from oesophagus and anus. Above: first portion is a control; the second is a curve taken after the left branch of the *A–V* bundle has been cut. Below: control and a curve taken after the right branch of the *A–V* bundle has been cut. After Rothberger and Eppinger.

severed, allowing impulses to reach only the left ventricle, the electrocardiogram immediately takes on another shape, the shape being an exaggeration of what occurs during enlargements of the left side of the heart. The first ventricular wave is sharp downward and the second an upward deflection. If, on the other hand, a similar injury is done to the conduction bundle to the right ventricle, there is a reversal of electrocardiographic curve. It consists of a sharp upward, followed by a downward deflection (Fig 6). Finally, if a curve of one or other form has been obtained by cutting one or other branch of the conducting bundle, one can, by severing the still uninjured branch, obtain an electrocardiogram which differs from both the preceding and resembles, though not exactly, the original curve. These changes depend, then, upon the way impulses pass through

the heart. An explanation of the nature of these abnormal curves is obtained by comparing them with others from hearts to which direct mechanical stimuli have been applied. A stimulus to the left side of the heart (ventricle) yields a curve like that seen when the right branch of the conducting bundle is cut, while one applied to the right side is like the curve seen when the left tract is cut. Under both conditions, contraction is initiated at the site of the stimulus, and the impulse spreads over the heart from this area. The form of the curve yielded depends on whether the right or left ventricle initiates the contraction.

The conduction bundle, then, is an important factor in the orderly cardiac mechanism, but, on account of its exposed position in the heart, it is frequently injured. The pathway between the auricles and the ventricles is, therefore, interrupted and impulses from one to the other are consequently blocked. The ventricles, deprived of stimuli from above, contract independently and without reference to the rate or rhythm of the auricular beats. In the study of derangements of the cardiac mechanism of this nature, electrocardiography has rendered distinct service.

So far we have discussed the mechanism of the heart-beat only in so far as it relates to the intrinsic arrangements of the heart. But for the proper exercise of a number of its functions, the heart is subjected to the influence of the central nervous system. In the study of this influence the galvanometer has been not only useful, but essential. Branches from the central nervous system to the heart exercise functions of two sorts,—inhibitory and accelerator. It has been especially our work to show that the inhibitory or slowing function is not simple and is not possessed equally by both vagus nerves. To say that the right vagus nerve principally modifies the rate of the heart and the left vagus chiefly conduction between its chambers states a truth and also indicates the presence of a complicated mechanism which may be explained in the following way: The complexity depends on the fact that the heart was originally an unpaired organ with a symmetrically distributed nerve supply. This supply, so far as we are informed, was directed to the junction between the old sinus venosus and the auricles. In the development of the heart, a division of the junctional tissue took place; one portion, the right,

remained at its original level, but became incorporated in the wall of the right auricle as the sinus node; the other portion, the left, became dislocated and moved downward the distance of a whole chamber, becoming, in the adult mammalian heart, the auriculo-ventricular node which lies between the auricles and the ventricles. The importance of these changes in position, from the point of view of innervation, lies in the fact that the cardiac branches of the two vagus nerves, which were distributed symmetrically in the primitive heart, have followed the changed positions of the structures they innervated originally and have become incorporated with them in their new situations. Consequently, the nodes and their nerves have assumed different functions. We were led to believe that this change must have taken place, first by clinical observation, and we have tested this hypothesis by experiment. As the result of experiments on many dogs, we were able to decide that when the right vagus nerve was electrically stimulated, the heart stopped beating. But when the left vagus nerve was stimulated, the auricles did not stop beating, but continued, though often at a slower rate. The striking thing now observed was that these auricular beats failed, either entirely or only occasionally, of being followed by a ventricular response (Plate II).

These were the facts. In the light of current teaching, the motions of the heart are initiated and rate is maintained by the sinus node. Impulses so initiated are conducted from the auricles to the ventricles over the narrow conduction path, with which we have become familiar. It follows that, when we find the heart stop as the result of a stimulus, we must assume the stimulus to have been distributed to that portion of the heart where the pace-making function resides, that is to say, at the sinus node. In the same way, when a disturbance in coördination between auricles and ventricles occurs, we have sufficient evidence to indicate that this occurs as the result of an effect produced at the junctional connecting tissues. We must, therefore, conclude that if stimulation of the left nerve brings about this disturbance, it must necessarily be distributed to this portion of the heart, that is to say, to the conducting system. Although we think that these sites, the sino-auricular and the auriculo-ventricular nodes, are the main terminals of these nerves, it is clear that other functions

are influenced at the same time when they are stimulated. We have indeed shown that this is the case. But our main concern has been to obtain information about essential differences; the likenesses and the additional influences exerted will be apparent. In this problem again, the galvanometer has been invaluable. On the basis of ordinary mechanical records, of which we have made many in the course of this work, we could not have drawn the conclusions just detailed.

Stimulation of the augmentor nerves shows that these have distributions similar to those of the inhibitors. Rothberger and Winterberg have contributed these facts. They have shown that stimulation of one or other augmentor nerve produces effects which can be referred to a modification of the function of the special cardiac tissues we have discussed in connection with the inhibitory nerves; and they have also shown that other differences of an electrocardiographic nature take place.

We have traced, in recording the newer aspects and methods of the study of the heart-beat, the influence exerted by the introduction of electrical methods. Advances by this method were due in large measure to the construction of an adequate galvanometer. But the advances in our understanding of the heart have depended on detailed anatomical and physiological investigation of the newly discovered structures in the heart itself. How small a portion it is that has been studied in relation to the whole heart, and how relatively few functions of the efficient organ have been included in the recent investigations, has been indicated. Much remains to be done by the means at our command, but much also by others still to be devised.

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